

Supporting Information

Regulating Transition-Metal Catalysis through Interference by Short RNAs**

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1. Materials and Methods

Unless stated otherwise, reactions were performed in flame-dried glassware under an atmosphere of nitrogen. Benzene, THF, dichloromethane, and dimethylformamide were degassed and dried in a JC Meyer solvent system. SilicaFlash P60 silicagel (230–400 mesh) was used for flash chromatography. NMR spectra were recorded on a Bruker AV-300 (1H), Bruker AV-400 (1H, 13C), Bruker DRX-500 (1H), and Bruker AV-500 (1H, 13C). 1H NMR spectra are reported relative to CDCl₃ (7.26 ppm). All oligonucleotides were purchased through Integrated DNA Technology with standard desalting unless otherwise specified. Samples for thermal denaturation, mass spectrometry studies, and catalysis were prepared by heating the buffered DNA solution without metal at 90 °C in a heating block for 10 minutes then cooled to room temperature for 30 minutes. Once cool, the metal solution was added. In thermal denaturation experiments, all absorbances were measured at 260 nm using HP-8453 spectrophotometer with HP-89090A Peltier temperature controller from 15–90 °C at 5 °C min⁻¹ with a hold time of 1 min. Relative absorbance, $A_{260nm} = (A_t - A_{15^\circ C}) / (A_{90^\circ C} - A_{15^\circ C})$, vs. temperature (°C) curves were fitted using GraphPad Prism 7.0c. Fluorescence experiments were recorded on a Tecan Infinite M1000 Pro plate reader with the following conditions: 480 nm excitation, 510 nm emission, 8 mm excitation and emission bandwidth, 50 flashes with a frequency of 400 Hz, and a 10 ms delay time. Fluorescence data was collected on a JASCO-J715 CD spectrophotometer with a scan rate of 20 nm/min from 200 nm to 300 nm with 3 accumulations. Mass spectrometry data was collected on a Thermo Scientific Q Exactive Plus Hybrid Quadrupole-Orbitrap Mass Spectrometer using negative ionization mode.

2.1 Thermal Stability Measurements

General Procedure for Sample Preparation for Thermal Stability Measurements

Solutions contained 3.5 μM DNA in buffer containing 0.75 mM sodium phosphate, pH 7, 150 mM NaClO_4 and 0 μM (0 eq) or 3.5 μM (1 eq) of $(\text{Me}_2\text{S})\text{AuCl}$ (60:1 $\text{H}_2\text{O}:\text{MeOH}$ v/v). DNA and buffer were heated at 90 $^\circ\text{C}$ for 10 minutes then allowed to cool to room temperature over 45 minutes. After the solution was cooled, $(\text{Me}_2\text{S})\text{AuCl}$ (210 μM stock solution in methanol) was added and the resulting solution was incubated at room temperature for 5 min before performing experiments. The reported data is based on 3 trials and graphed on GraphPad Prism 7.0c.

Table S1. Sequences used in thermal denaturation experiments:

Sequence Name	Strand 1	Strand 2
CT1	5'-GAG GGA CAG AAA GG-3'	5'-CCT TTC TTT CCC TC-3'
AT1	5'-GAG GGA AAG AAA GG-3'	5'-CCT TTC TTT CCC TC-3'
CG1	5'-GAG GGA CAG AAA GG-3'	5'-CCT TTC TGT CCC TC-3'
CTH	5'-CGT TCT GTT TTC AGC ACG-3'	N/A
TAH	5'-CGT TCT GTT TTC AGA ACG-3'	N/A

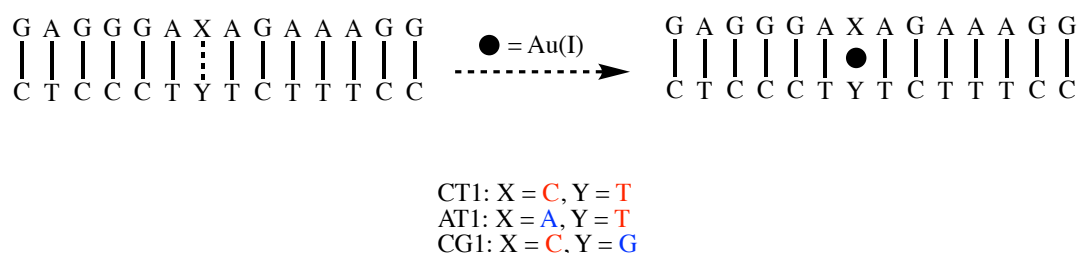
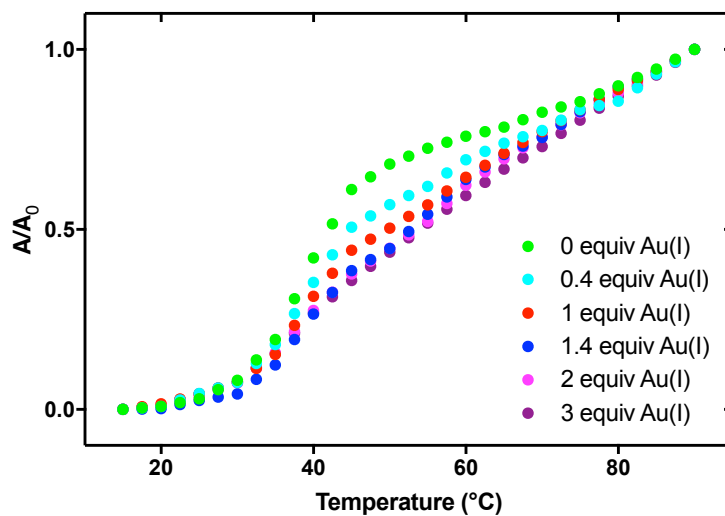


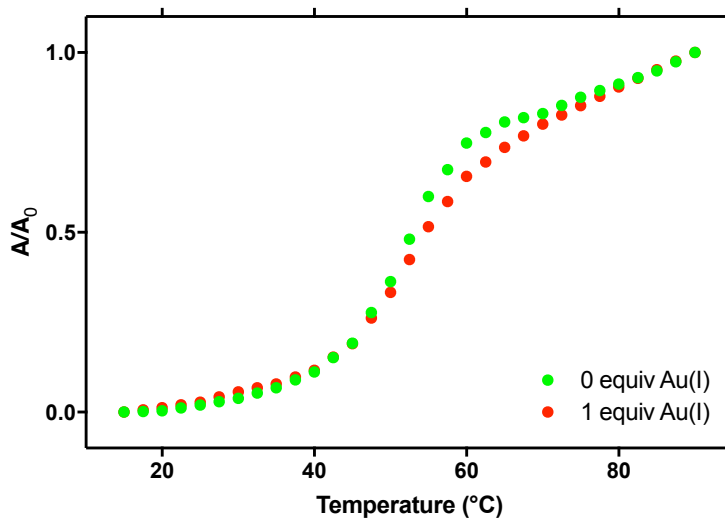
Figure S1. Duplex mismatch sequences with and without gold.

Thermal denaturation profiles of CT1, AT1, CG1, CTH, and TAH in the presence of (Me₂S)AuCl

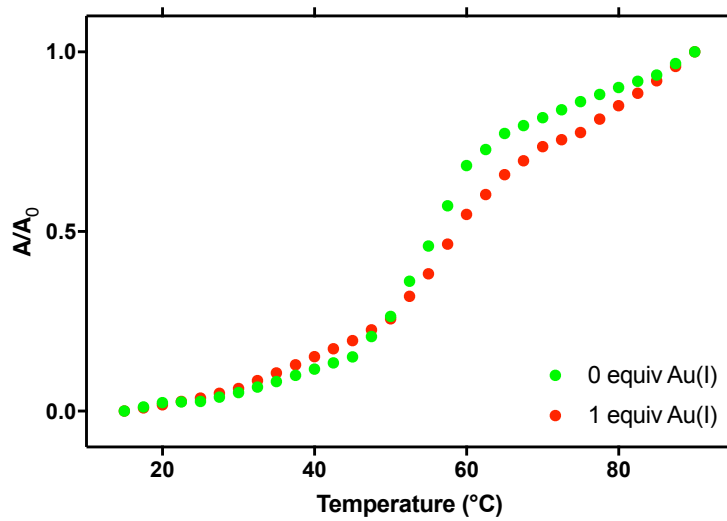
a) CT1



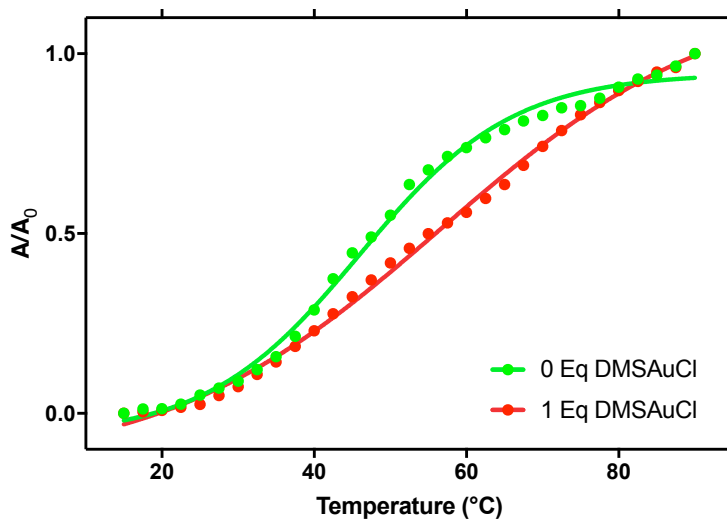
b) AT1



c) CG1



d) CTH



e) TAH

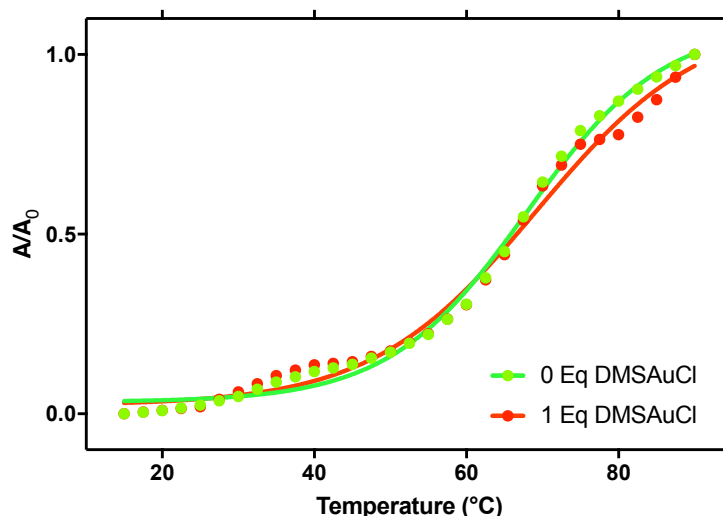


Figure S2. Relative absorbance, $A_{260nm} = (A_t - A_{15^\circ C}) / (A_{90^\circ C} - A_{15^\circ C})$, vs. temperature ($^\circ C$) curves for pyrimidine-mismatch-containing oligonucleotides, a) CT1 b) AT1 c) CG1, d) CTH, and e) TAH in the presence of $(Me_2S)AuCl$. CTH and TAH show sigmoidal fit curves. Solutions contained $3.5 \mu M$ DNA in buffer containing 0.75 mM sodium phosphate, pH 7, 150 mM $NaClO_4$ and $1.4 \mu M$ (0.4 equiv), $3.5 \mu M$ (1 equiv), $4.9 \mu M$ (1.4 equiv), $7 \mu M$ (2 equiv) or $10.5 \mu M$ (3 equiv), $(Me_2S)AuCl$ ($60:1$ $H_2O:MeOH$ v/v).

Table S2. Thermal denaturation values for CT1 sequence

Thermal Denaturation – CT1			
[Au]	T_m ($^\circ C$)	ΔT_m ($^\circ C$)	Error
0 equiv	40.6	--	0.7
0.4 equiv	42.7	2.1	1.0
1 equiv	47.3	6.7	1.1
1.4 equiv	50.7	10.1	0.6
2 equiv	51.3	10.7	0.6
3 equiv	53.2	12.6	1.8

Table S3. Thermal denaturation values for control sequences AT1, CG1, CTH, TAH

Thermal Denaturation – AT1 and GC1				
Sequence	0 equiv T_m ($^\circ C$)	1 equiv T_m ($^\circ C$)	ΔT_m ($^\circ C$)	Error
AT1	52.4	53.8	1.4	0.4
GC1	55.6	60.0	4.4	0.6
CTH	45.9	56.6	10.7	1.1
TAH	67.9	69.2	1.3	2.1

Melting temperatures calculated from the thermal denaturation profiles of pyrimidine-mismatch-containing oligonucleotides in the presence of various concentrations of $(Me_2S)AuCl$. Melting temperatures and error calculated using the sigmoidal dose-response feature in GraphPad Prism 7.0c.

Thermal denaturation profiles of pyrimidine-mismatch-containing oligonucleotides in the presence of various Au precursors

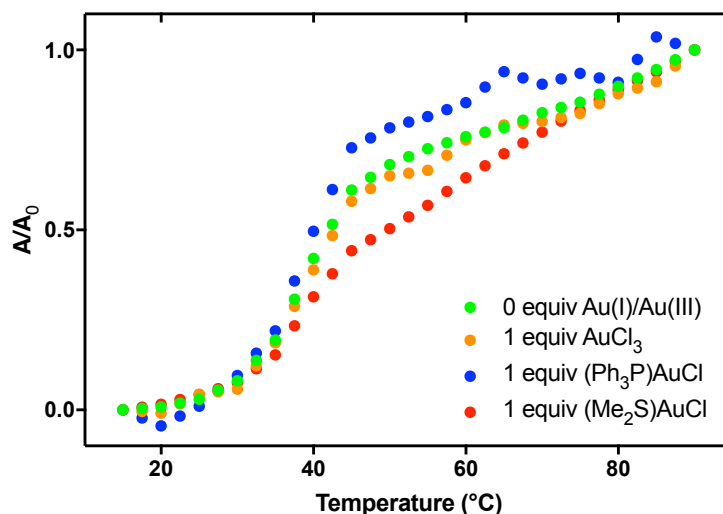


Figure S3. Relative absorbance, $A_{260\text{nm}} = (A_t - A_{15^\circ\text{C}}) / (A_{90^\circ\text{C}} - A_{15^\circ\text{C}})$, vs. temperature ($^\circ\text{C}$) curves for pyrimidine-mismatch-containing oligonucleotides, CT1, in the presence of $(\text{Me}_2\text{S})\text{AuCl}$, AuCl_3 or $(\text{Ph}_3\text{P})\text{AuCl}$. Solutions contained $3.5 \mu\text{M}$ DNA in buffer containing 0.75 mM sodium phosphate, $\text{pH } 7$, 150 mM NaClO_4 and $3.5 \mu\text{M}$ (1 equiv) of Au precursor: $(\text{Me}_2\text{S})\text{AuCl}$, AuCl_3 or $(\text{Ph}_3\text{P})\text{AuCl}$ (60:1 $\text{H}_2\text{O}:\text{MeOH}$ v/v).

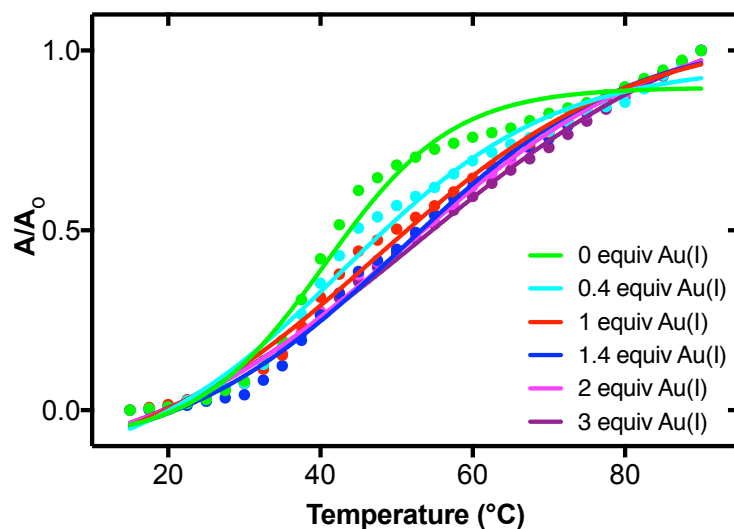
Table S4. Thermal denaturation values of CT1 with different gold precursors.

Thermal Denaturation – CT1			
Gold Precursor	T_m ($^\circ\text{C}$)	ΔT_m ($^\circ\text{C}$)	Error
No Au	40.6	—	0.7
$(\text{Me}_2\text{S})\text{AuCl}$	47.3	6.7	1.1
$(\text{Ph}_3\text{P})\text{AuCl}$	39.3	0.9	0.6
AuCl_3	41.2	0.6	1.2

Melting temperatures calculated from the thermal denaturation profiles of pyrimidine-mismatch-containing oligonucleotides in the presence of 1 equivalent of various gold precursors. Melting temperatures and error calculated using the sigmoidal dose-response feature in GraphPad Prism 7.0c.

Thermal denaturation profiles of pyrimidine-mismatch-containing oligonucleotides at with fits from GraphPad Prism showing sigmoidal fit and biphasic fit.

a) sigmoidal fit of CT1 at various equivalents of (Me₂S)AuCl



b) biphasic fit of CT1 at various equivalents of (Me₂S)AuCl

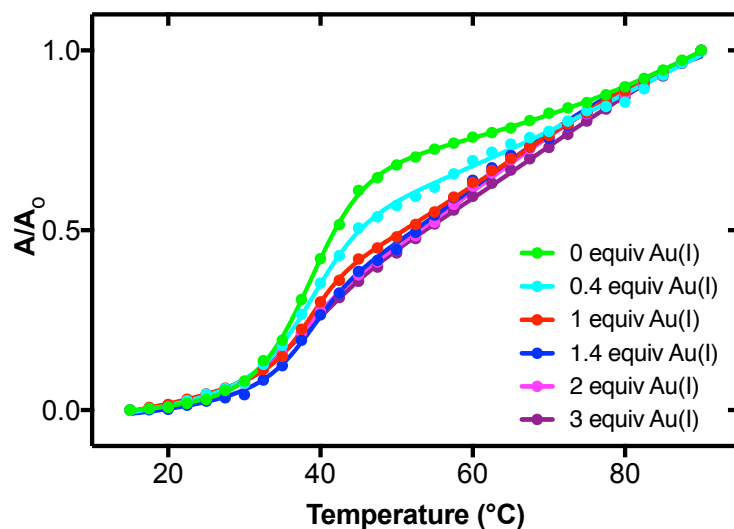


Figure S4. Relative absorbance, $A_{260nm} = (A_t - A_{15^\circ C}) / (A_{90^\circ C} - A_{15^\circ C})$, vs. temperature (°C) curves for pyrimidine-mismatch-containing oligonucleotides, CT1, in the presence of (Me₂S)AuCl fit using a) sigmoidal fit and b) biphasic fit. Solutions contained 3.5 μ M DNA in buffer containing 0.75 mM sodium phosphate, pH 7, 150 mM NaClO₄ and 3.5 μ M (1 equiv) of (Me₂S)AuCl. (60:1 H₂O:MeOH v/v).

Table S5. Thermal denaturation values for CT1 sequence based on biphasic fit

Thermal Denaturation – CT1				
[Au]	T_{m1} (°C)	T_{m2} (°C)	Error (T_{m1})	Error (T_{m2})
0 equiv	38.7	N/A	0.2	N/A
0.4 equiv	38.9	85.4	0.3	11.3
1 equiv	38.6	62.6	0.7	3.2
1.4 equiv	38.9	61.7	0.5	2.0
2 equiv	37.9	60.8	0.6	2.2
3 equiv	39.0	68.8	2.4	12.8

Thermal denaturation profiles of pyrimidine-mismatch-containing oligonucleotides at pH 5.5 and pH 8.5.

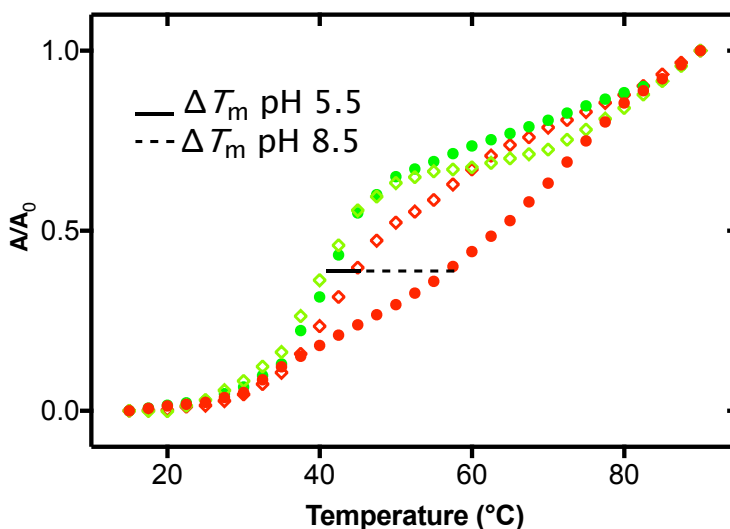


Figure S5. Relative absorbance, $A_{260nm} = (A_t - A_{15^\circ C}) / (A_{90^\circ C} - A_{15^\circ C})$, vs. temperature (°C) curves for pyrimidine-mismatch-containing oligonucleotides, CT1, in the presence of $(Me_2S)AuCl$ at various pH solutions. Solutions contained 3.5 μM DNA in buffer containing 0.75 mM sodium phosphate, pH 5.5 or 8.5, 150 mM $NaClO_4$ and 3.5 μM (1 equiv) of Au precursor: $(Me_2S)AuCl$, $AuCl_3$ or $(Ph_3P)AuCl$ (60:1 $H_2O:MeOH$ v/v).

2.2 Circular Dichroism (CD)

General Procedure for Sample Preparation for Circular Dichroism Spectroscopy

Solutions contained 3.5 μM DNA in buffer containing 0.75 mM sodium phosphate, pH 7, 150 mM NaClO_4 and 0 μM (0 equiv) or 3.5 μM (1 equiv) of $(\text{Me}_2\text{S})\text{AuCl}$ (60:1 $\text{H}_2\text{O}:\text{MeOH}$ v/v). DNA and buffer were heated at 90 $^\circ\text{C}$ for 10 minutes then allowed to cool to room temperature over 45 minutes. After the solution was cooled, 5 μl of $(\text{Me}_2\text{S})\text{AuCl}$ (210 μM stock solution in methanol) was added and the resulting solution was incubated at room temperature for 5 min before performing experiments. The reported data is based on 3 trials and graphed on GraphPad Prism 7.0c.

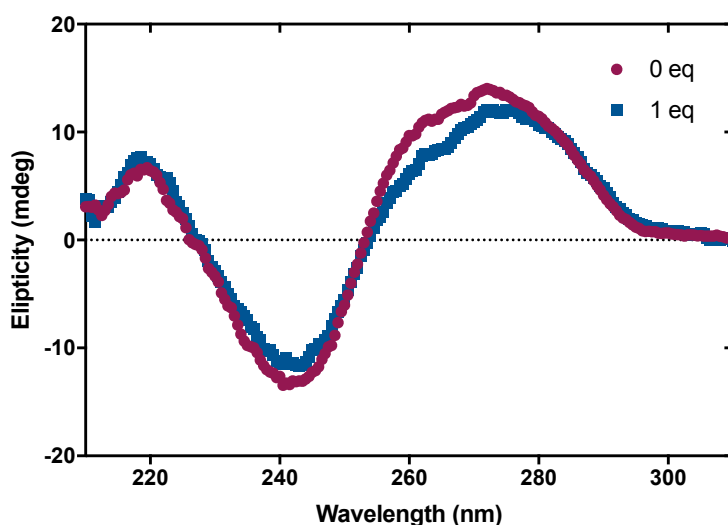


Figure S6. CD spectra of CT1 duplex in the presence of 0 equiv (0 eq) or 1 equiv (1 eq) $(\text{Me}_2\text{S})\text{AuCl}$.

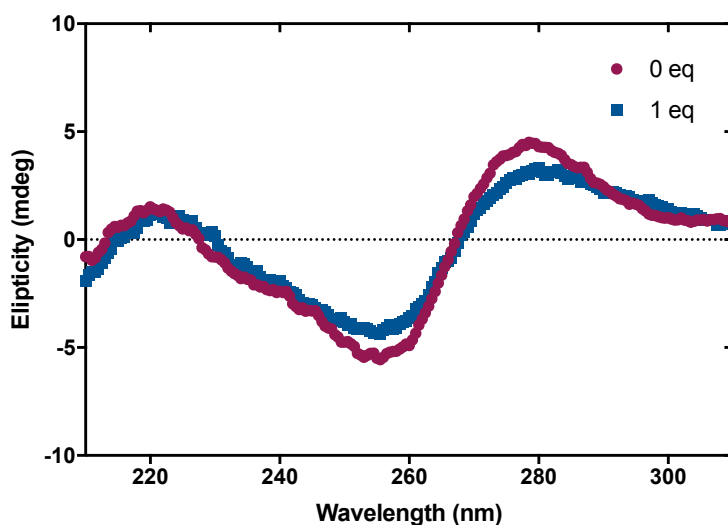


Figure S7. CD spectra of CTH1 hairpin in the presence of 0 equiv (0 eq) or 1 equiv (1 eq) Me_2SAuCl .

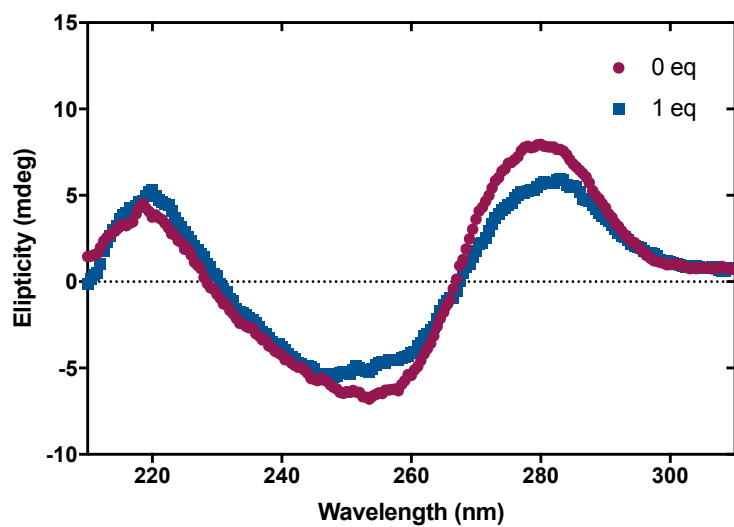


Figure S8. CD spectra of TAH hairpin in the presence of 0 equiv (0 eq) or 1 equiv (1 eq) Me_2SAuCl .

2.3 Mass Spectrometry

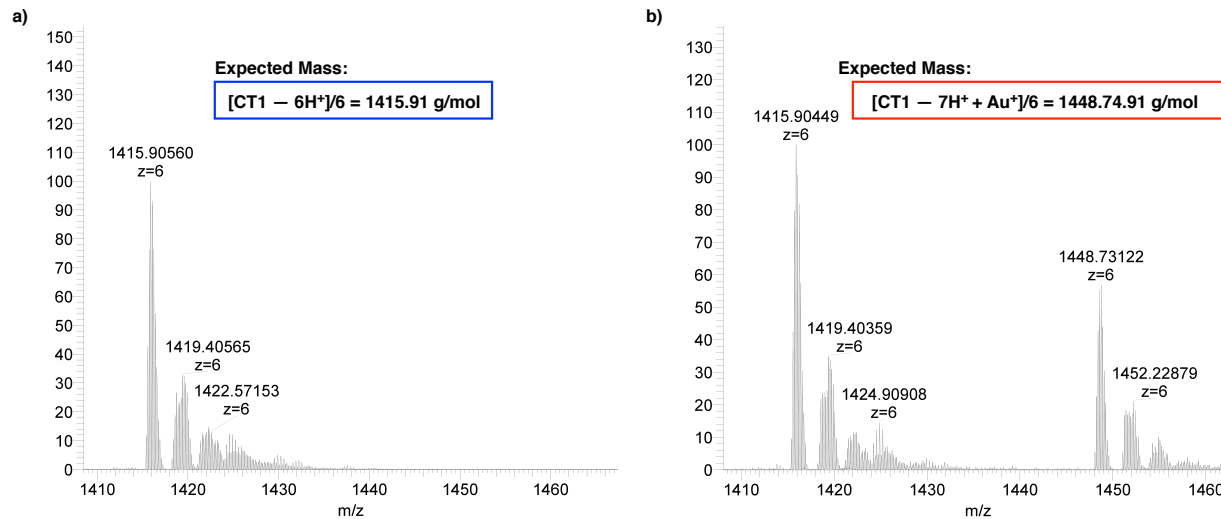


Figure S9. Mass spectrometry of CT1 sequence a) without $(\text{Me}_2\text{S})\text{AuCl}$, and b) with 1 equivalent $(\text{Me}_2\text{S})\text{AuCl}$ ($5 \mu\text{M}$). Solutions contained $5 \mu\text{M}$ CT1, 50 mM NH_4OAc in 4:1 $\text{H}_2\text{O}:\text{MeOH}$ v/v.

3. DNA-Au(I) Hydroamination Reactions

3.1 General Procedure

Samples for catalysis were prepared by heating the buffered DNA solution without metal at 90 °C in a heating block for 10 minutes. After 10 minutes, the solutions were cooled to room temperature over 30 minutes. Once cool, the metal solution was added. Following metal addition, the complement sequence was added and the solution was allowed to equilibrate for 10 minutes before adding it to a solution of BODIPY **7** in ethanol resulting in a final solution containing (1:1:0.02 H₂O:EtOH:(CH₃)₂CO). Reactions contain 10 μM DNA hairpin, 10 μM complement sequence, 250 mM or 62.5 mM NaClO₄ and 40 μM BODIPY **7**. All other conditions/concentrations vary depending on experiment. Positive control contains no DNA. Negative control contains no DNA nor (Me₂S)AuCl. No comp (0 eq): 0 equivalents of complement sequence added to reaction. Comp (1 eq): 1 equivalent (10 μM) complement sequence added to reaction. Progress of reactions was determined by fluorescence intensity. All fluorescence values reported in arbitrary units. Fold increase in fluorescence was calculated based on equation $FI = (F_{1eq} - F_{0eq}) / (F_{0eq})$. Yields were calculated using a standard curve of product BODIPY **8** at known concentrations ranging from 3.25 μM to 60 μM, this was then fit to a line in excel and the equation was used to calculate the yield of fluorescent product for each reaction.

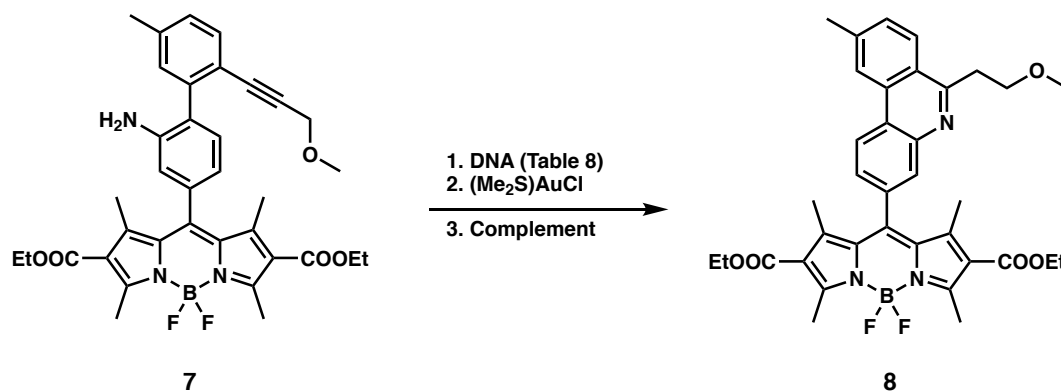
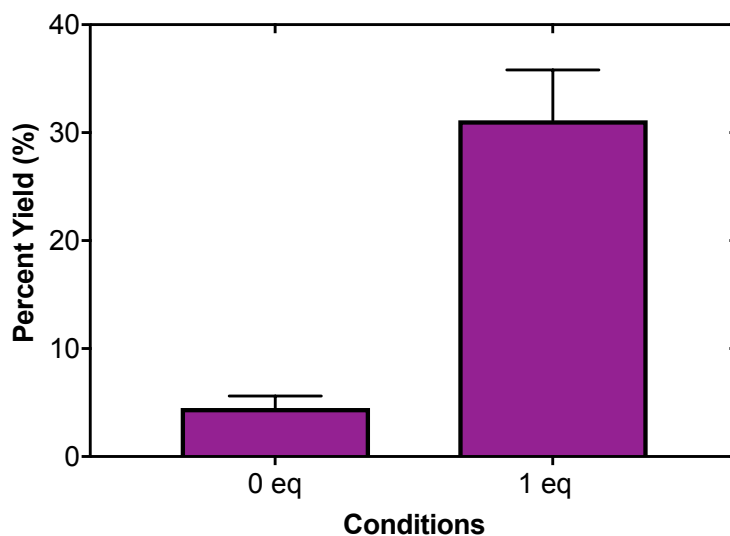


Figure S10. Gold catalyzed hydroamination reaction¹.

Table S6. Sequences used in catalysis experiments.

Sequence Name	Sequence
CTH5	5'-CGT TCT GTT TTC AGC ACG ACA TC-3'
cCTH5	5'-GAT GTC GTG CTG AAA AC-3'
cCTH5-5s	5'-GAT GTC GTG ATG AAA AC-3'
cCTH5-5d	5'-GAT GTC GGG ATG AAA AC-3'
cCTH5-3s	5'-GAT GTC GTG CTG AAA AA-3'
cCTH5-3d	5'-GAT GTC GTG CTG AAA GA-3'
cCTH5-TMs	5'-GAT ATC GTG CTG AAA AC-3'
cCTH5-TMd	5'-GAG ATC GTG CTG AAA AC-3'
RcCTH5	5'-GAU GUC GUG CUG AAA AC-3'
CGH5	5'-CGT GCT GTT TTC AGC ACG ACA TC-3'

3.2 Fluorescence Data

**Figure S11.** Calculated percent yield of standard conditions based on standard curve with no cCTH5 added (0 eq) and 1 equivalent of cCTH5 added (1 eq) to hairpin CTH5.

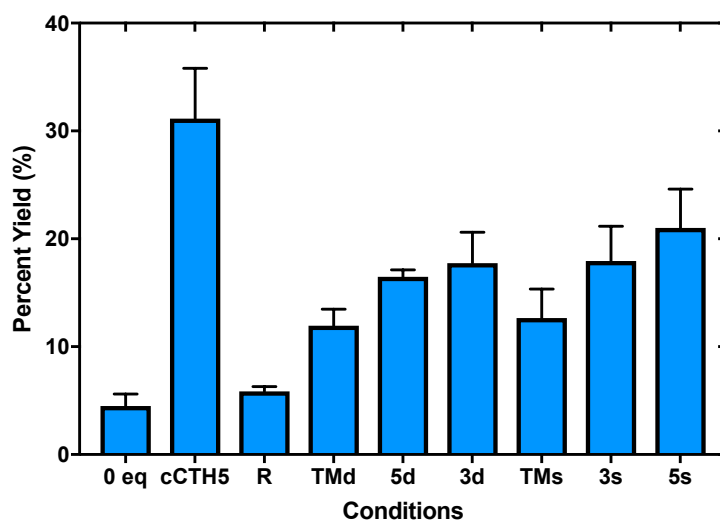


Figure S12. Percent yields of product with perfect complement (cCTH5) and various mismatched complements (R, TMd, 5d, 3d, TMs, 3s, 5s) at 250 mM sodium perchlorate.

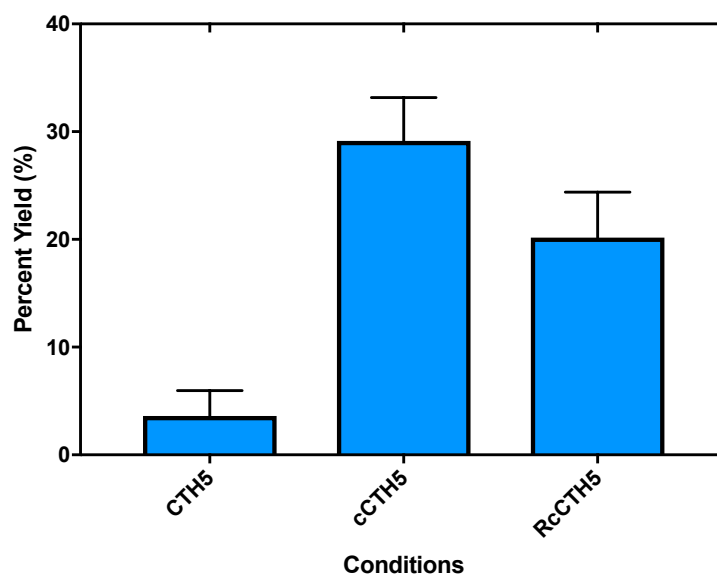


Figure S13. Calculated percent yield of standard conditions for hairpin sequence CTH5 with no added complement (CTH5), with 1 equivalent cCTH5 (cCTH5), and with 1 equivalent of RNA complement (RcCTH5).

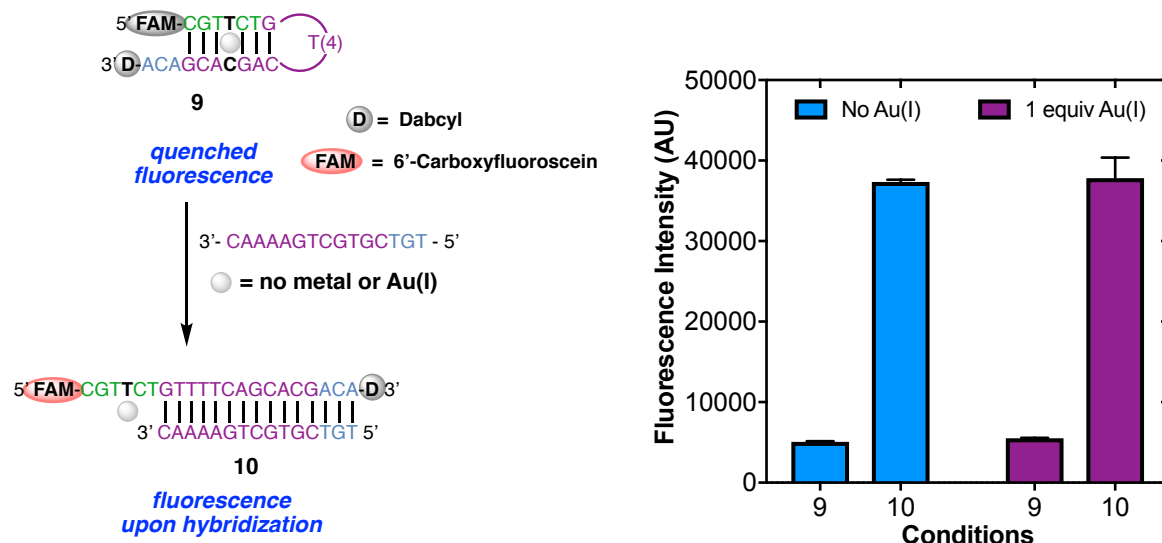


Figure S14. Control experiment showing hybridization still occurs in the presence of Au(I).

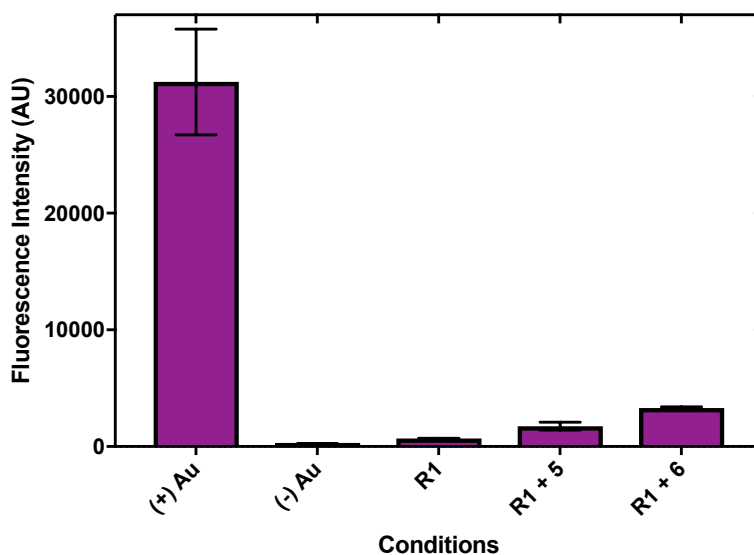


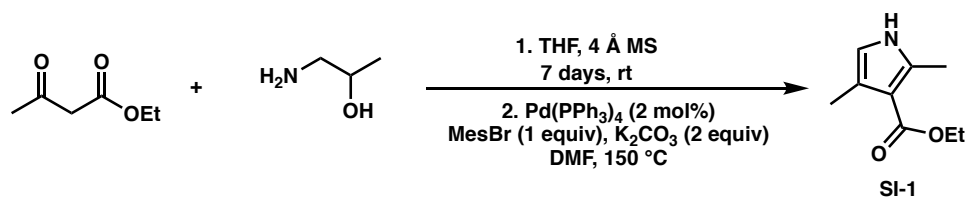
Figure S15. Results showing that random sequence R1 results in low levels of fluorescence. (+) Au: only (Me₂S)AuCl, (-) Au: no (Me₂S)AuCl, R1: R1 and (Me₂S)AuCl, R1 + 5: R1, (Me₂S)AuCl, and CTH5 (5), R1 + 6: R1, (Me₂S)AuCl, CTH5 and cCTH5 (6).

Preparation of experiments containing biologically relevant fluids

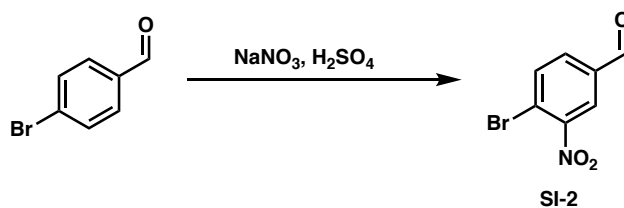
Solutions contain 10 μ M DNA hairpin, 10 μ M complement sequence, and 62.5 mM NaClO₄ and 40 μ M BODIPY 7 with 10 μ M R1, or 30 % solutions of synthetic saliva (Artificial Saliva for Medical and Dental Research purchased through Pickering Laboratories) or synthetic urine (300 mM urea, 60 mM KCl, 128 mM NaCl, 30 mM Na₃PO₄, 15 mM creatine, and 1 μ M albumin powder).

4. Synthesis

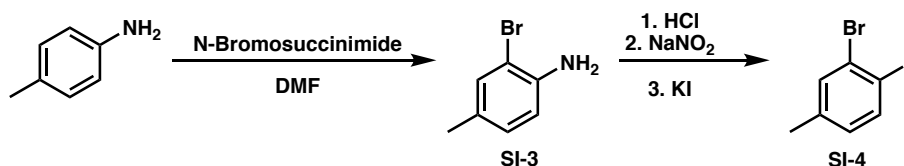
4.1 Synthesis of BODIPY derivative (7)



3,5-dimethyl-4-(ethoxycarbonyl)pyrrole (SI-1): Synthesized according to reported literature. NMR spectra match those reported in literature².

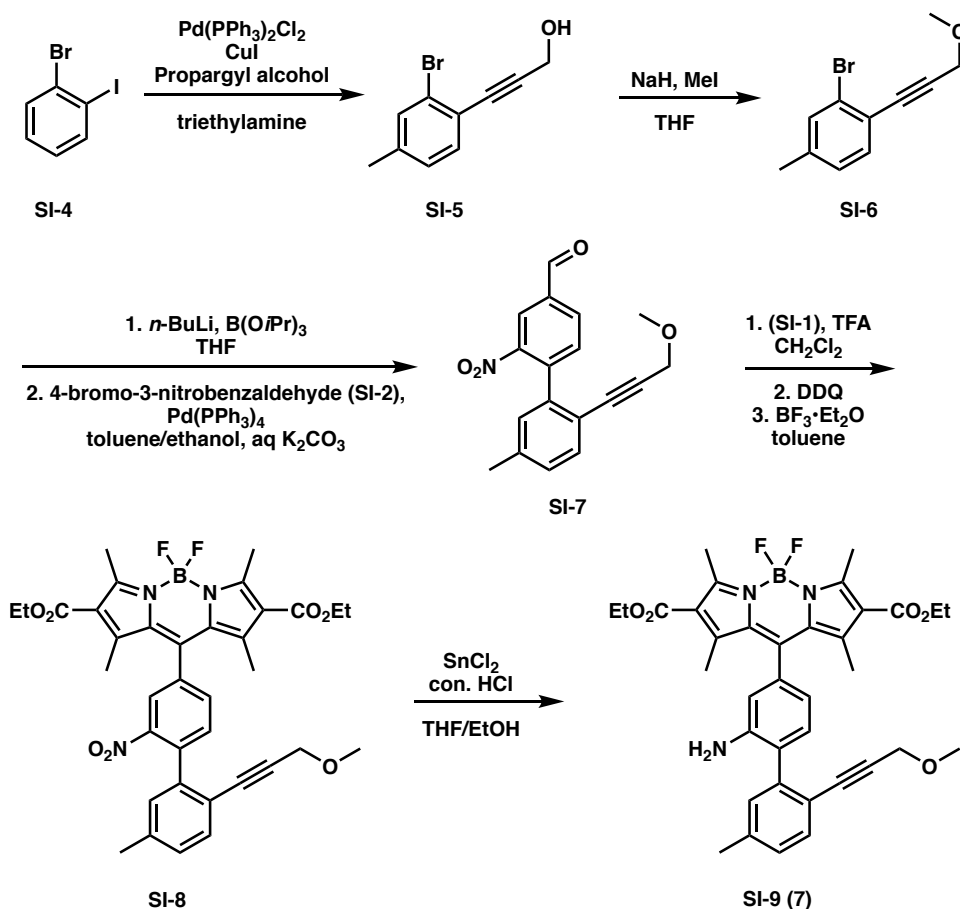


4-bromo-3-nitrobenzaldehyde (SI-2): Synthesized from 4-bromobenzaldehyde according to reported literature. NMR spectra match those reported in literature³.



2-bromo-4-methylaniline (SI-3): Synthesized from 4-methylaniline according to reported literature. NMR spectra match those reported in literature⁴.

2-bromo-4-methyl-iodobenzene (SI-4): Synthesized according to reported literature. NMR spectra match those reported in literature⁴.



3-(2-bromo-4-methylphenyl)prop-2-yn-1-ol (SI-5): Synthesized from 2-bromo-4-methyliodobenzene according to reported literature. NMR spectra match those reported in literature¹.

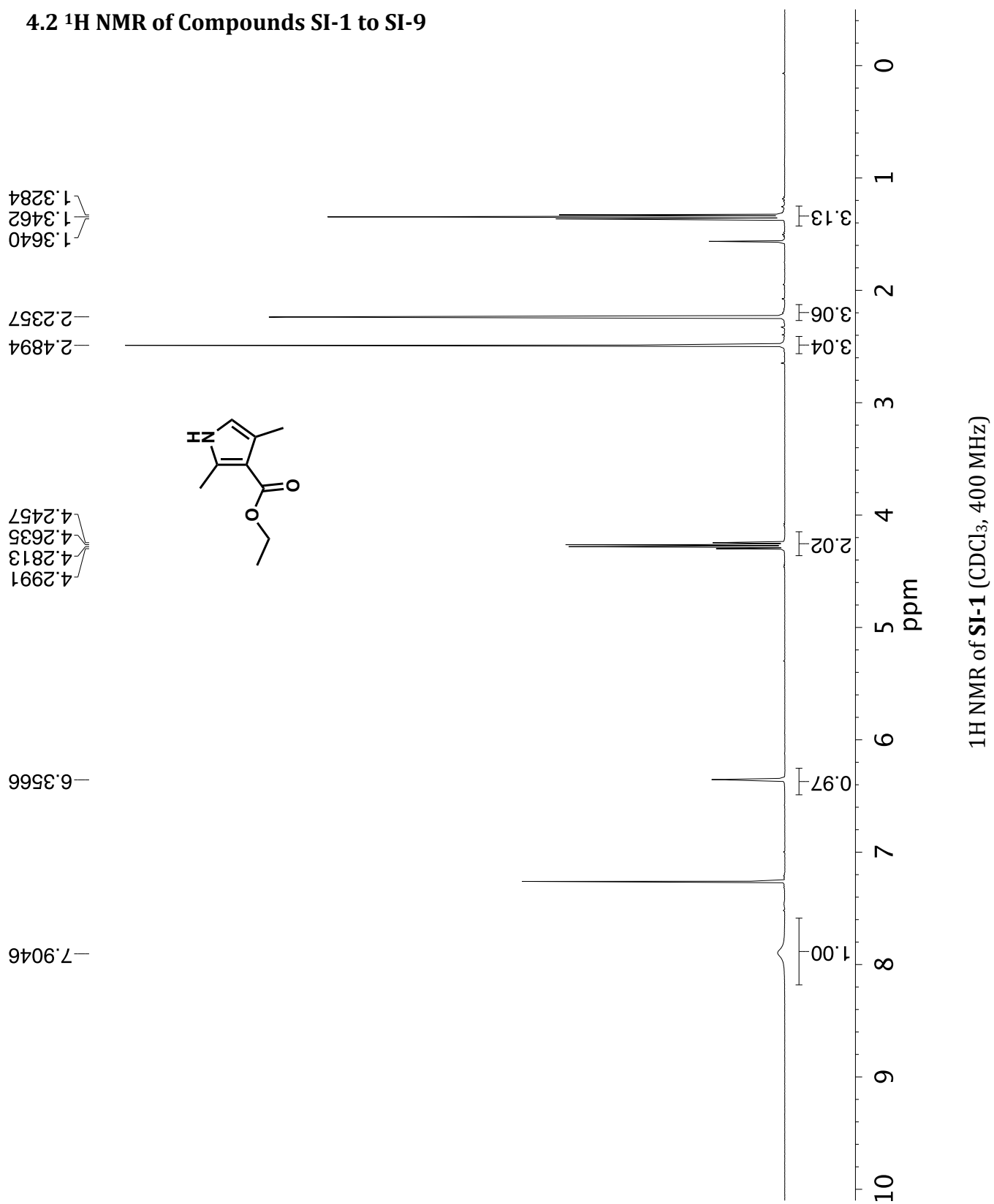
2-bromo-1-(3-methoxyprop-1-ynyl)-4-methylbenzene (SI-6): Synthesized from 3-(2-bromo-4-methylphenyl)prop-2-yn-1-ol according to reported literature. NMR spectra match those reported in literature¹.

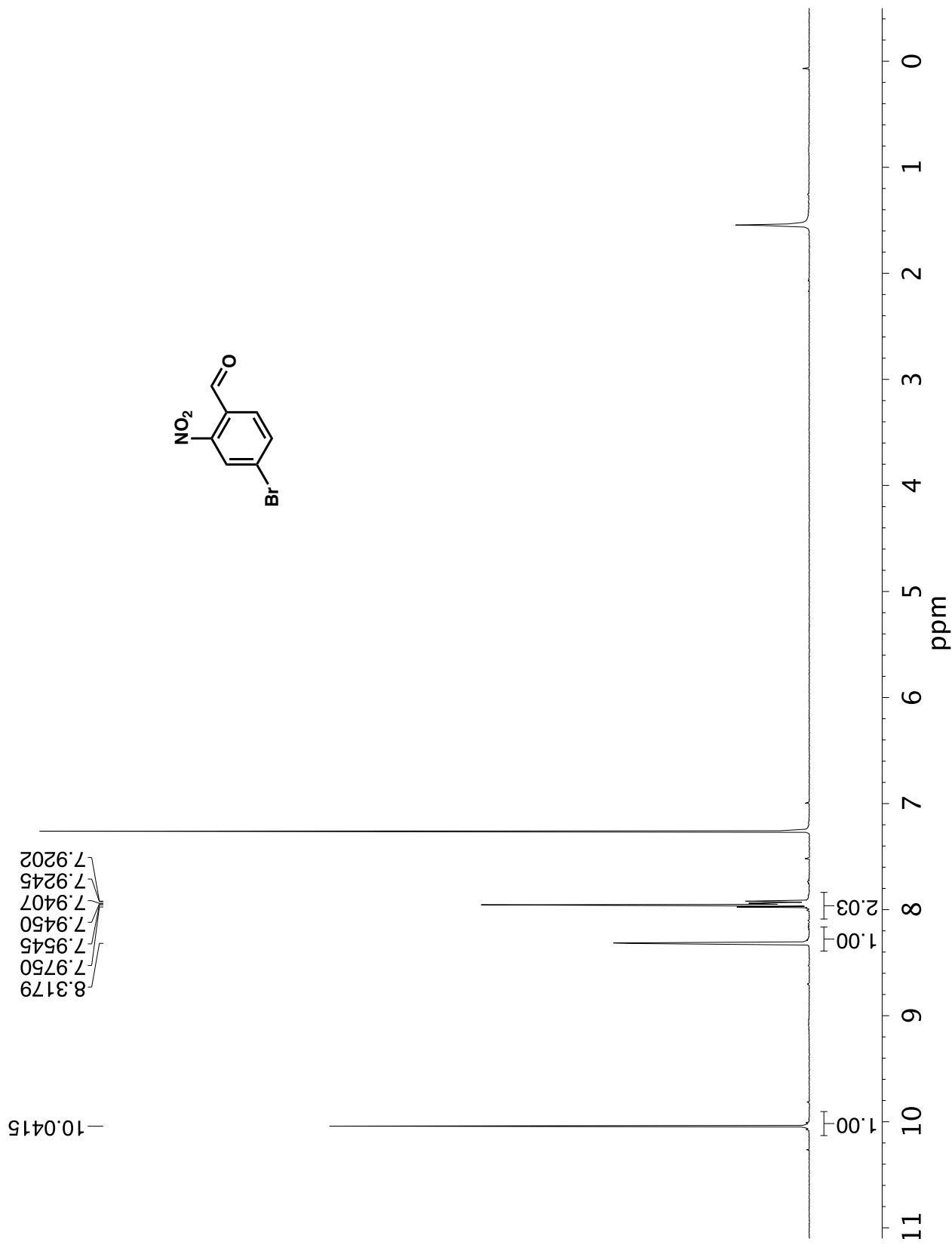
2'-(3-methoxyprop-1-yn-1-yl)-5'-methyl-2-nitro-[1,1'-biphenyl]-4-carbaldehyde (SI-7): Synthesized from 4-bromobenzaldehyde according to reported literature. NMR spectra match those reported in literature¹.

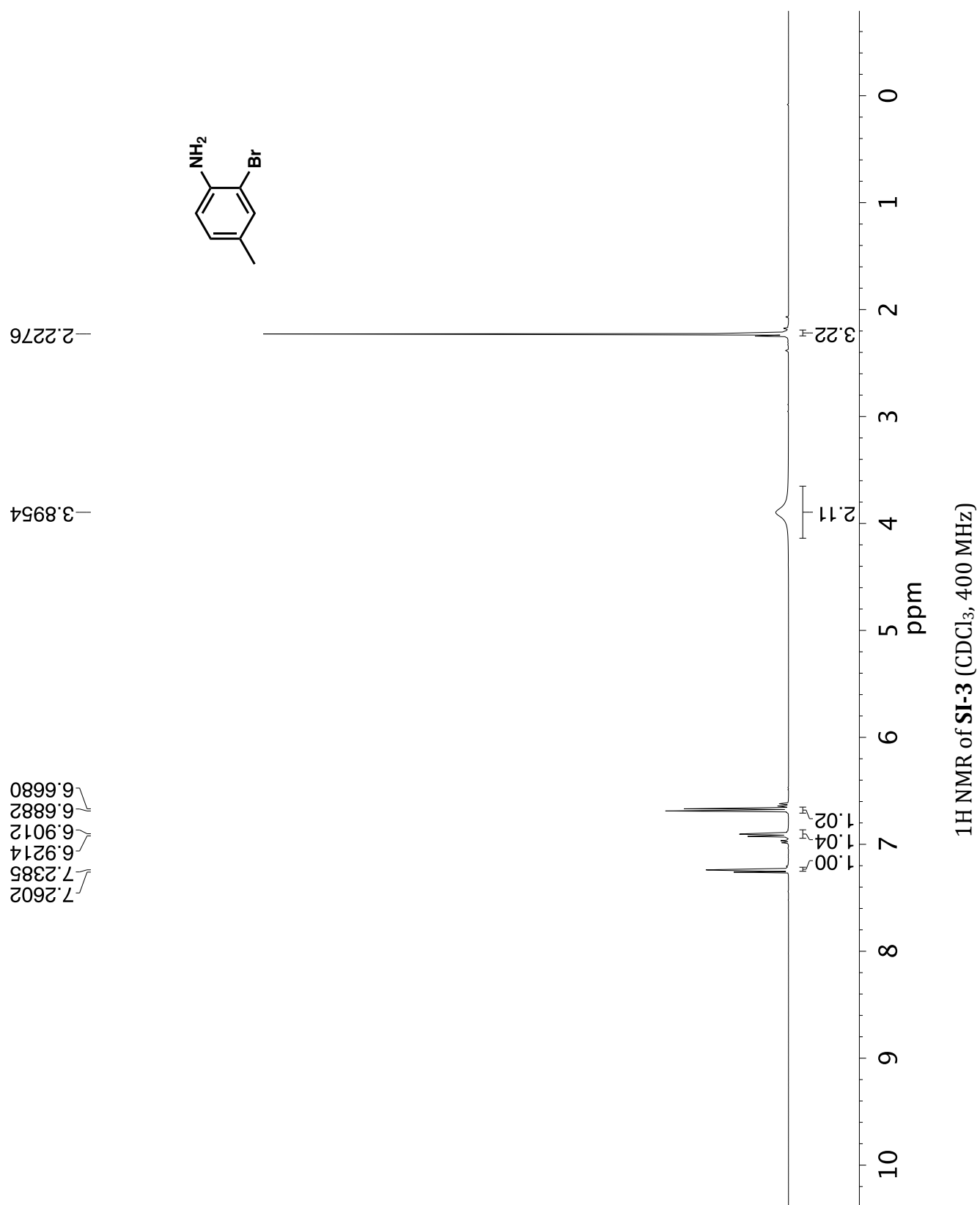
2,8-bis(ethoxycarbonyl)-5,5-difluoro-10-(2'-(3-methoxyprop-1-yn-1-yl)-5'-methyl-2-nitro-[1,1'-biphenyl]-4-yl)-1,3,7,9-tetramethyl-5H-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-4-ium-5-uide (SI-8): Synthesized according to reported literature. NMR spectra match those reported in literature¹.

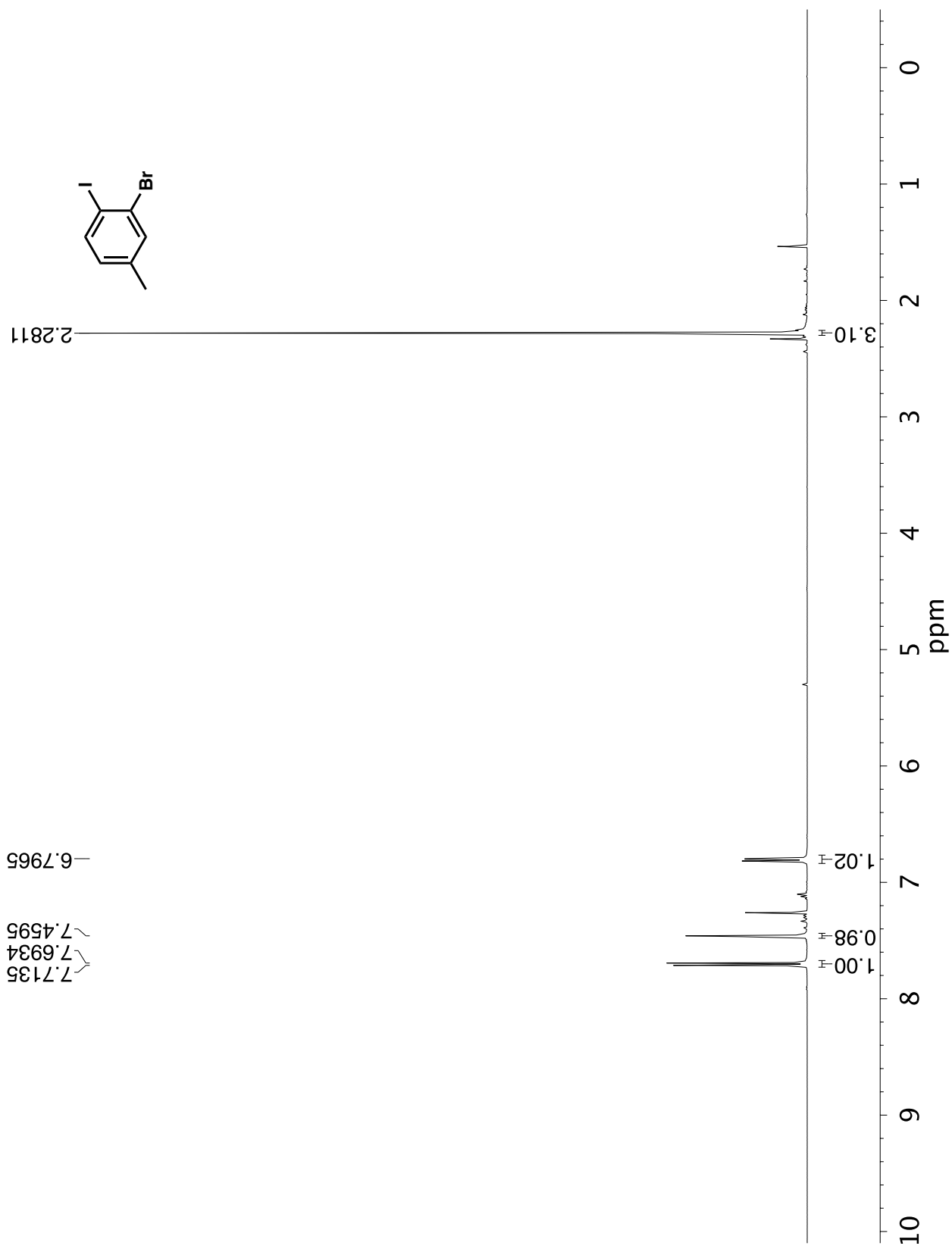
2,8-bis(ethoxycarbonyl)-5,5-difluoro-10-(6-(2-methoxyethyl)-9-methylphenanthridin-3-yl)-1,3,7,9-tetramethyl-5H-dipyrrolo[1,2-c:2',1'-f][1,3,2]diazaborinin-4-ium-5-uide (SI-9): Synthesized according to reported literature. NMR spectra match those reported in literature¹.

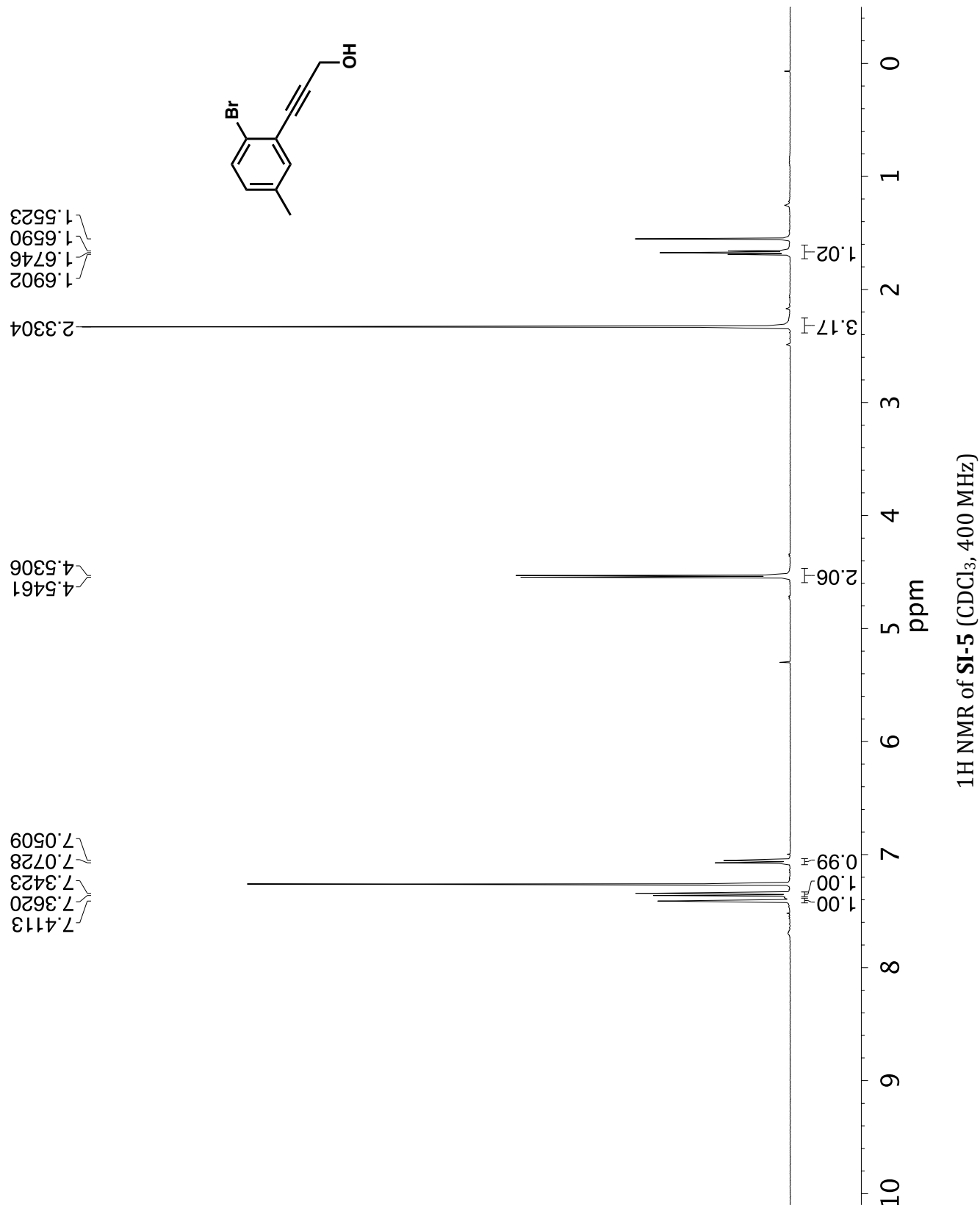
4.2 ^1H NMR of Compounds SI-1 to SI-6



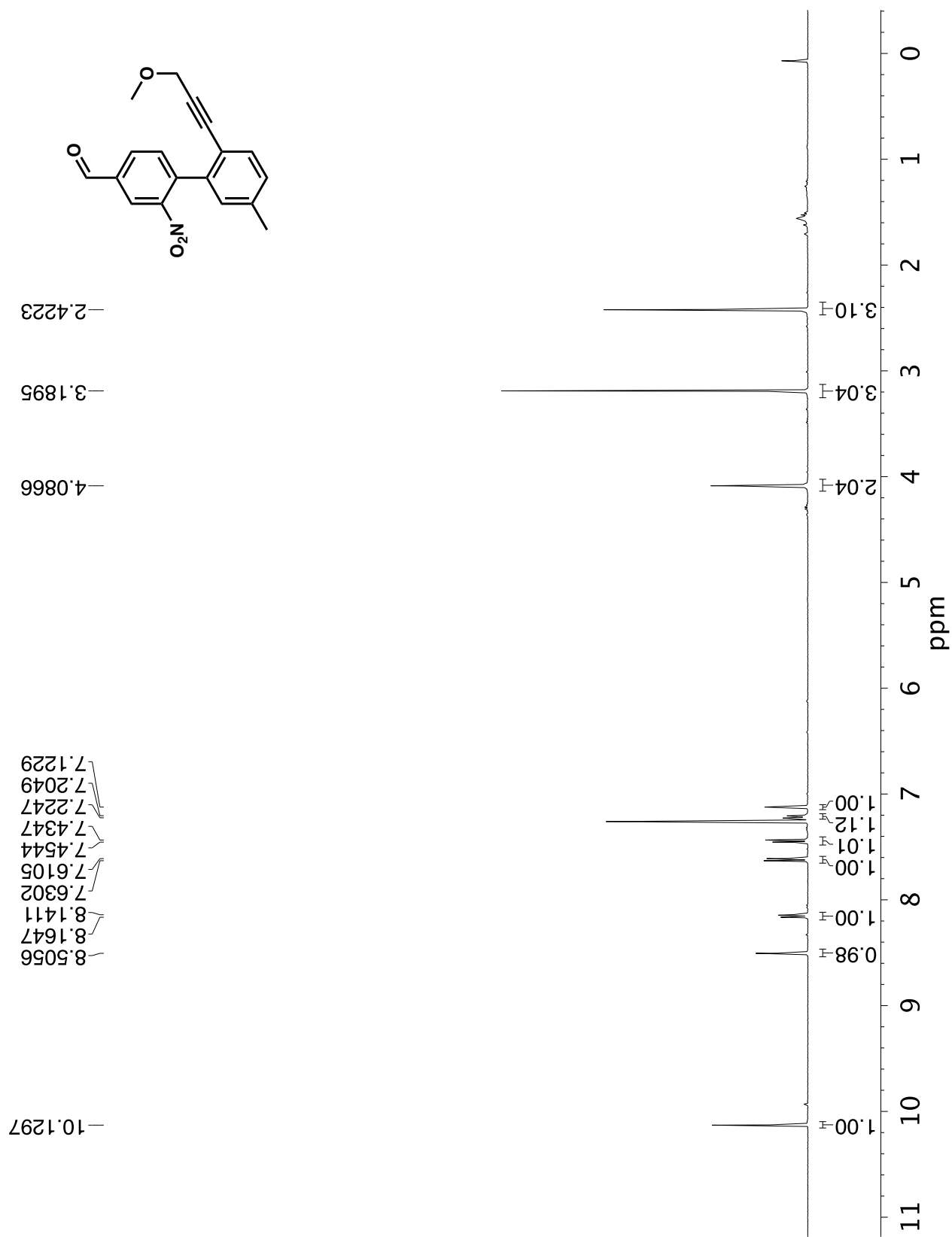
^1H NMR of **SI-2** (CDCl_3 , 400 MHz)



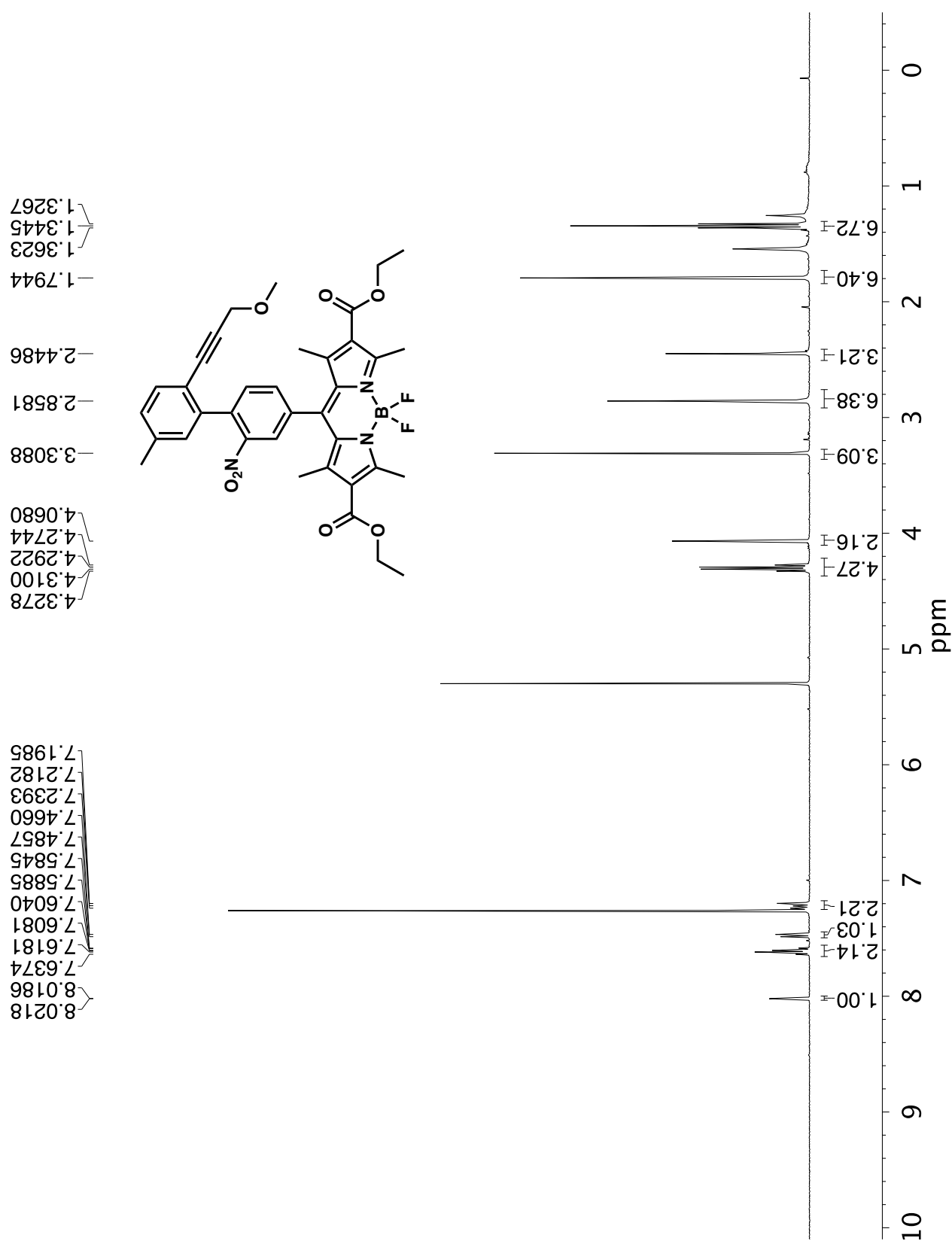
^1H NMR of SI-4 (CDCl_3 , 400 MHz)



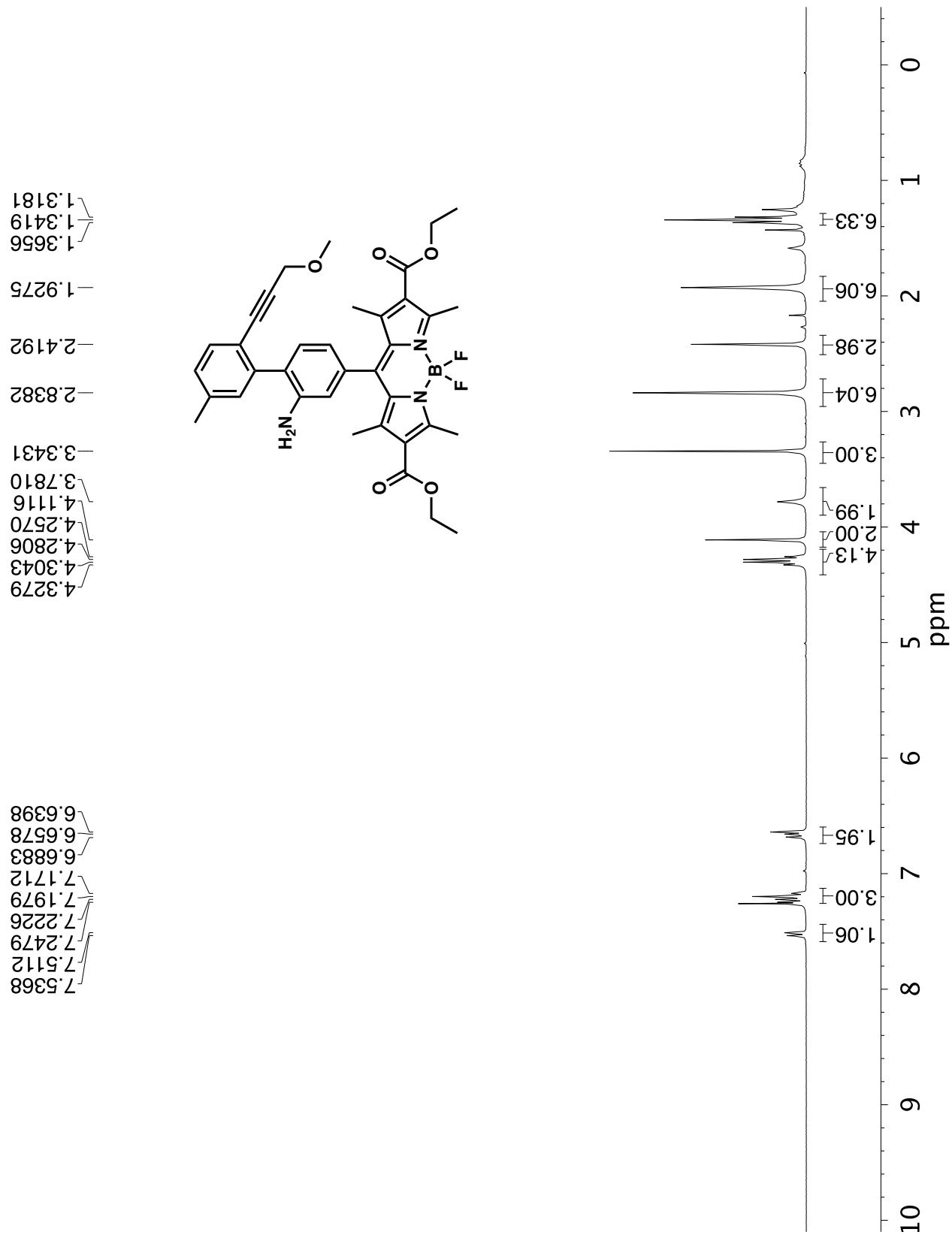
^1H NMR of SI-6 (CDCl_3 , 400 MHz)

^1H NMR of SI-7 (CDCl_3 , 400 MHz)

¹H NMR of **SI-8** (CDCl₃, 400 MHz)



¹H NMR of **SI-9** (CDCl₃, 400 MHz)



6. References

1. Wang, J., Wu, Q., Min, Y., Liu, Y. & Song, Q. A novel fluorescent probe for Au(III)/Au(I) ions based on an intramolecular hydroamination of a Bodipy derivative and its application in bioimaging. *Chem. Commun.* **48**, 744–746 (2012).
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4. Lv, J., Liu, Q., Tang, J., Perdih, F. & Kranjc, K. A facile synthesis of indolo[3,2,1-*jk*]carbazoles via palladium-catalyzed intramolecular cyclization. *Tetrahedron Lett.* **53**, 5248–5252 (2012).